REMARKS

The present document is submitted in reply to the Office Action dated August 27, 2007 ("Office Action").

Applicants have amended claims 5 and 6 to promote clarity. Support for the amendments appears in claim 2.[1] Further, Applicants have added new claims 40-45, support for which can be found at various places in the specification, e.g., at page 5, lines 19-20; and page 16, Table 2. Finally, Applicants have cancelled claims 7-9 and 14. No new matter has been introduced.

Upon entry of the present amendments, claims 2-6, 10, 11, 13, 15-18, and 21-45 will be pending. Among them, claims 17, 18, and 21-38 have been withdrawn from consideration and claims 2-6, 10, 11, 13, 15, 16, and 39-45 will be examined.

Applicants respectfully request that the Examiner reconsider this application in view of the following remarks.

New Matter Rejection

Claims 2-6, 10, 11, 13, 15, 16, and 39 stand rejected for including new matter on three grounds, which are addressed separately below.

A

The Examiner asserts that the present specification does not adequately support an antigen-presenting cell (APC) targeting molecule that "includes a **Class II MHC binding site**," as recited in independent claim 2. See page 3, third paragraph; and pages 5-6, section 7. Applicants respectfully disagree.

The law is well settled that whether a phrase recited in a claim is supported by the specification shall be determined based on what the specification is reasonably communicated to those skilled in the art. See MPEP § 2163.05, citing *In re Wilder*, 222 USPQ 369, 372 (Fed. Cir., 1984). Indeed, the phrase at issue does not have to be set forth verbatim in the specification. In *In re Wright*, 9 USPQ2d 1649 (Fed. Cir. 1989), the

[1] The Examiner has questioned whether the present specification provides sufficient support for two terms recited in claim 2. Applicants will discuss this issue below.

Federal Circuit, in reversing a Board's 35 U.S.C. § 112, first paragraph rejection, held that there was adequate written description support for the applicant's claim limitation, despite the fact that it was not set forth "*in haec verba*" (i.e., "in these words" or "verbatim") in the specification.

In this case, claim 2 covers a conjugate containing an antigen coupled to an APC-targeting molecule, which includes a **Class II MHC binding site** and a T-cell receptor binding site of a superantigen. The T-cell receptor binding site is mutated at one or more positions such that it displays a reduced T-cell proliferation activity.

The specification explicitly points out that the APC-targeting molecule recited in claim 2 "mimics a superantigen but does not include a fully functional T-cell receptor binding site" and "is structurally a superantigen **but for** a disrupted T-cell binding site ..." See page 3, lines 4-12. In view of these teachings, a skilled person in the art would readily know that the APC-targeting molecule included in the claimed conjugate is a mutated superantigen having a mutation(s) **only** in its T-cell receptor binding site.

It is well known in the art that superantigens, belonging to a conserved protein family, are capable of stimulating T cells via binding to **Class II MHC molecules** and T cell receptors. See Arcus et al., *J. Mol. Biol.*, 299:157-168 (2000) and Leder, et al., J. Exp. Med., 187:823-833 (1998); copies attached as Exhibits A and B. Structurally, all superantigens contain two functional domains, i.e., a **Class II MHC binding site** and a T-cell receptor binding site. See Exhibit A, page 158, left column, fourth paragraph; and page 160, left column, last paragraph. In view of these teachings, a skilled person in the art would readily know that a superantigen mutant having a mutation(s) **only** in its T-cell receptor binding site definitely includes a **Class II MHC binding site**, which is a common functional domain of all superantigens.

In sum, the specification teaches that the APC-targeting molecule recited in claim 1 is a **superantigen mutant** containing one or more mutations only in its T cell binding domain, which, according to the aforementioned common knowledge about superantigens, includes a **Class II MHC binding site**. Thus, pursuant to the caselaw

quoted above, the specification provides adequate support for an APC-targeting molecule that "includes **a Class II MHC binding site** of a superantigen," as required by claim 2.

For a complete record, Applicants address below the Examiner's argument in support of this rejection. The Examiner asserts that "[t]he instant specification discloses a molecule [an APC-targeting molecule as that recited in claim 2] that is structurally a superantigen, **but for** a disrupted T cell receptor binding site," and that "structurally a superantigen might include proteins that exhibit a high degree of homology to a supernatigen, but would not necessarily require a MHC class II binding site." See pages 3-4, bridging paragraph. Applicants would like to point out that the Examiner has obviously overlooked the term **"but for"** in one of the two above-quoted phrases "a molecule that is structurally a superantigen **but for** a disrupted T cell receptor binding site." The use of this term in the just-quoted phrase clearly excludes superantigen mutants that contain mutations in regions other than their T-cell binding sites, e.g., **Class II MHC binding sites**. In other words, contrary to the Examiner's position, the APC-targeting molecule recited in claim 2 necessarily requires a **Class II MHC binding site**, which is a common domain of all superantigens. See the discussion at page 9, supra.

B

The Examiner deems that the present specification does not provide adequate support for the clause "the T cell binding site having one or more mutations that reduce its T cell proliferation activity" recited in claim 2. More specifically, it is the Examiner's position that the specification generally discloses "molecules that lose **T cell activation activity**," but not "molecules that have reduced **T cell proliferation activity**." Applicants respectfully disagree.

It is well known in the art that, all activated T cells undergo clonal expansion, i.e., proliferation. See Abbas et al., Cellular and Molecular Immunology, page 164, Figure 8-2 (copy attached as Exhibit C). Indeed, a molecule's ability to activate T cells is commonly indicated by its ability to induce T cell proliferation. See, e.g., Exhibit B, page 828, left column, second paragraph; and right column, Figure 3. In other words, "T

cell activating activity" and "T cell proliferation activity" are synonymous to a skilled person in the art.

As pointed out above, the present specification discloses a molecule that "mimics a superantigen but does not include "**a fully functional T-cell receptor binding site.**" See page 3, lines 4-7. In view of this teaching, a skilled artisan would readily understand that the specification teaches a superantigen containing mutations in its T-cell binding site such that, compared to its wild-type counterpart, the superantigen exhibits reduced **T-cell activation or proliferation activity**. Applicants thus submit that, in accordance with the law quoted at pages 8-9 above (bridging paragraph), the specification fully supports the clause at issue.

C

Finally, the Examiner asserts that the term "reduces the T cell proliferation activity to equal to or greater than **10,000 fold**" recited in claim 39 does not have support in the specification.

Applicants would like to bring to the Examiner's attention two teachings in the specification. First, the specification teaches a superantigen mutant having no ability to activate T-cells. See page 3, line 12. Second, the specification further teaches that "[a] fully ablated TcR binding negative superantigen [having no ability to activate T-cells] is defined herein as one that displays less than about 0.0001% of proliferative activity of the wild-type superantigen." See page 16, lines 12-15. In view of these two teachings, a skilled artisan would know that a superantigen mutant having no ability to activate T cells, i.e., having a fully ablated TcR binding site, displays greater than 10,000 fold reduction of T cell proliferation activity compared to its wild-type counterpart. In other words, the specification fully supports the term in question.

In view of the above remarks, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection under 35 U.S.C. 112, First Paragraph (Written Description)

The Examiner rejects claim 5 and its dependent claim 6 for lack of written description. Previously presented claim 5 covers a conjugate containing an APC-targeting molecule derived from *Staphylococcus arueus* and/or *Streptococcus pyogenes*. The Examiner holds that term "derived from *Staphylococcus arueus and/or Streptococcus pyogenes*" is overly broad as it encompasses any protein expressed in *Staphylococcus arueus and/or Streptococcus pyogenes* that targets an APC cell. See the Office Action, pages 4-5, section 6.

Applicants have narrowed claim 5 to "a mutated superantigen of *Staphylococcus arueus and/or Streptococcus pyogenes*." Amended claim 5 no longer encompasses any protein of *Staphylococcus arueus* and/or *Streptococcus pyogenes* that targets an APC cell; rather, it requires a mutated superantigen of *Staphylococcus arueus and/or Streptococcus pyogenes*. Applicants thus submit that this amendment has rendered moot the Examiner's ground for rejection.

For the sole purpose of facilitating prosecution, Applicants have also amended claim 6 to clarify that it requires a mutant SPE-C, which is a superantigen of *Staphylococcus arueus and Streptococcus pyogenes*. Thus, the just-mentioned ground for rejection does not apply to amended claim 6.

Rejection under 35 U.S.C. 103

Claims 2-6, 10, 11, 13, 15, 16, and 39 are rejected as obvious over McCormick et al. J. Immunology, 165:2306-2312 ("McCormick") in view of Capon et al., US Patent 5,116,964 ("Capon"). See the Office Action, pages 6-7, section 8.

Independent claim 2 will be discussed first. As pointed out above, this claim covers a conjugate containing two components: (1) an APC-targeting molecule coupled with (2) an antigen. The APC targeting molecule is a superantigen mutant, whose T-cell receptor binding site is disrupted.

According to the Examiner, McCormick discloses a number of mutants of SPEC, a superantigen, and Capon teaches fusing a stable plasma protein to a protein ligand to increase the half-life of the ligand. See the Office Action, page 6, last paragraph; and

page 7, second paragraph. The Examiner thus concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings in McCormick and Capon, i.e., fusing a stable plasma protein as taught in Capon to one of the superantigen mutants taught in McCormick, thereby reaching the conjugate of claim 2. Applicants respectfully disagree.

Applicants would like to first point out the following two facts:

(1) In the conjugate of claim 2, the two components, i.e., the superantigen mutant and the antigen (e.g., the stable plasma protein mentioned in Capon), do not merely perform the functions when they act separately, as taught in McCormick and Capon. When functioning separately, the McCormick superantigen mutants act as **vaccine proteins** that induce immune responses against themselves (see Abstract), and the Capon stable plasma protein, an antigen, **increases the half-life** of a protein ligand to which it is fused (see column 5, lines 13-18). In the claimed conjugate, the superantigen mutant and the stable plasma act as an **adjuvant** that facilitates induction of an immune response against the stable plasma protein and as a strong **immunogenic antigen**, respectively. See the specification, page 6, lines 13-30; and pages 22-25, Example 8. Clearly, the two components of the claimed conjugate perform **unpredictable** functions in this conjugate.

(2) The bioactivity of the conjugate covered by claim 2 was unexpected in view of both McCormick and Capon. As pointed out above, Capon teaches that fusing the stable plasma protein disclosed therein with a protein partner increases the half-life of the protein partner. Accordingly, a skilled person in the art would have expected that fusing the stable plasma protein with one of the superantigen mutants disclosed in McCormick would stabilize the superantigen mutant in vivo. He or she certainly would have expected that the stable plasma protein would be **non-immunogenic**, as otherwise, it would be rapidly eliminated via the immune response it induces. Surprisingly, the claimed conjugate is capable of inducing a strong immune response against its antigen component, e.g., the stable plasma protein. In other words, the antigen in the conjugate of claim 2 is **highly immunogenic**, an unexpected feature of this conjugate.

It is well settled that the above two facts are evidence that can be relied on to rebut the obviousness rejection. See, e.g., the Examination Guidelines for Determining Obviousness under 35 U.S.C. 103, Section V, provided by the US Patent and Trademark Office. These guidelines set forth that, to rebut an obviousness rejection of a claim to a combination, "applicants may submit evidence or argument to demonstrate that: (1) ... (2) the elements in combination do not merely perform the function that each element performs separately; or (3) the results of the claimed combination were unexpected." See Section V; emphasis added. Applicants thus submit that, given these two facts, the conjugate of claim 2 is nonobvious over McCormick and Capon, either taken alone or in combination. So are claims 3-6, 10, 11, 13, 15, 16, and 39, all of which depend from claim 2, directly or indirectly.

New claims 40-45 depend ultimately from claim 2. For at least the same reasons set forth above, they are also not obvious over McCormick and Capon.

CONCLUSION

It is believed that all of the pending claims have been addressed. However, the absence of a reply to a specific rejection, issue or comment does not signify agreement with or concession of that rejection, issue or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

The Petition for Extension of Time fee in the amount of $ 525 is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges to Deposit Account No. 50-4189, referencing Attorney Docket No. 55503-002001.

Respectfully submitted,

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